# Serial No.: 10/699,597 Filed: October 30, 2003

#### IN THE CLAIMS:

Please cancel claims 19-28. Please add claims 39 - 41.

This listing of claims will replace all prior version and listings of claims in the application.

## **Listing of Claims**

- 1. A cardiac specific-synthetic promoter produced by a method comprising: (Original)
  - (a) introducing a library of randomized synthetic-promoter-recombinant expression constructs into a first-population of cells forming a first-test-population of cells;
  - (b) screening the first-test-population of cells for a first cardiac-specific-clone having a first-transcriptional activity that is higher than a control-transcriptional activity; and
  - (c) utilizing the cardiac specific-synthetic promoter from the first-cardiac-specific clone as the cardiac specific-synthetic promoter for a cardiac-specific-synthetic expression construct;

wherein,

each of the randomized synthetic-promoter-recombinant expression constructs are operatively linked to a reporter gene to form a nucleic acid expression construct; and

the control-cardiac-specific-clone comprises a known-promoter operatively linked to the reporter gene forming a control-nucleic acid expression construct having the control-transcriptional activity in the first-population of cells.

2. (Original) The cardiac specific-synthetic promoter of claim 1, wherein the firstpopulation of cells comprise cells in vitro.

3. (Original) The cardiac specific-synthetic promoter of claim 1, further comprising: second-screening the first cardiac-specific-clone in a second-testpopulation of cells before utilizing the cardiac-specific-synthetic promoter as the cardiac-specific-synthetic promoter for the cardiac-specific-synthetic expression construct;

wherein,

the reporter gene from the first-cardiac-specific-clone having a second-transcriptional activity in the second-population of cells that is higher than a second-control-transcriptional activity of the control-cardiac-specific-clone introduced into the second-population of cells.

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- 4. **(Original)** The cardiac specific-synthetic promoter claim 3, wherein the first-population of cells comprise cells *in vitro*, and the second-population of cells comprise cells *in vivo*.
- 5. **(Original)** The cardiac specific-synthetic promoter of claim 1, wherein cardiac specific synthetic promoter comprises c5-12 (SeqID#5).
- 6. **(Original)** The cardiac specific-synthetic promoter of claim 1, wherein cardiac specific synthetic promoter comprises c1-26 (SeqID#16); c2-26 (SeqID#17); c2-27 (SeqID#18); c5-5 (SeqID#19); c6-5 (SeqID#20); c6-16 (SeqID#21); or c6-39 (SeqID#22).
- 7. **(Original)** The cardiac specific-synthetic promoter of claim 1, wherein the cardiac-specific-synthetic promoter comprises a first-combination of cis-acting regulatory elements;

the first combination of cis-acting regulatory elements being selected from library of randomized synthetic-promoter-recombinants; and

the cardiac-specific synthetic promoter driving a transcriptional activity of the expressible gene in a population of cells that is higher than the transcriptional

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activity of the expressible gene driven by a control-promoter in the population of cells.

- 8. **(Original)** The cardiac specific-synthetic promoter of claim 7, wherein the cis-acting regulatory elements comprise SRE (SeqID#1); MEF-1 (SeqID#2); MEF-2 (SeqID#3); and TEF-1 (SeqID#4).
- 9. **(Original)** A method of using a cardiac specific-synthetic expression construct for expressing a gene in a cardiac cell comprising:

delivering into the cardiac cell a cardiac specific-synthetic expression construct; wherein, the cardiac-specific-synthetic expression construct comprises a cardiac-specific-synthetic-promoter operatively-linked to an expressible gene.

- 10. **(Original)** The method of claim 9, wherein cardiac specific synthetic promoter comprises c5-12 (SeqID#5).
- 11. **(Original)** The method of claim 9, wherein cardiac specific synthetic promoter comprises c1-26 (SeqID#16); c2-26 (SeqID#17); c2-27 (SeqID#18); c5-5 (SeqID#19); c6-5 (SeqID#20); c6-16 (SeqID#21); or c6-39 (SeqID#22).
- 12. **(Original)** The method of claim 9, wherein the cardiac-specific-synthetic promoter comprises a first-combination of cis-acting regulatory elements;

the first combination of cis-acting regulatory elements being selected from library of randomized synthetic-promoter-recombinants; and

the cardiac-specific synthetic promoter driving a transcriptional activity of the expressible gene in a population of cells that is higher than the transcriptional activity of the expressible gene driven by a control-promoter in the population of cells.

- 13. **(Original)** The method of claim 12, wherein the cis-acting regulatory elements comprise SRE (SeqID#1); MEF-1 (SeqID#2); MEF-2 (SeqID#3); and TEF-1 (SeqID#4).
- 14. **(Original)** The method of claim 9, wherein delivering into the cardiac cell the cardiac specific-synthetic expression construct is via electroporation.

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- 15. **(Original)** The method of claim 9, wherein the expressible-gene comprises a nucleic acid sequence that encodes a growth-hormone-releasing-hormone ("GHRH") or functional biological equivalent thereof.
- 16. **(Original)** The composition of claim 15, wherein the encoded GHRH is a biologically active polypeptide, and the encoded functional biological equivalent of GHRH is a polypeptide that has been engineered to contain a distinct amino acid sequence while simultaneously having similar or improved biologically activity when compared to the GHRH polypeptide.
- 17. **(Original)** The method of claim 15, wherein the encoded GHRH or functional biological equivalent thereof is of formula (SEQID#6):

$$-X_{-1}$$
- $X_2$ -DAIFTNSYRKVL- $X_3$ -QLSARKLLQDI- $X_4$ -

## X<sub>5</sub>-RQQGERNQEQGA-OH

wherein the formula has the following characteristics:

 $X_1$  is a D-or L-isomer of the amino acid tyrosine ("Y"), or histidine ("H");

X<sub>2</sub> is a D-or L-isomer of the amino acid alanine ("A"), valine ("V"), or isoleucine ("I");

X<sub>3</sub> is a D-or L-isomer of the amino acid alanine ("A") or glycine ("G");

X<sub>4</sub> is a D-or L-isomer of the amino acid methionine ("M"), or leucine ("L");

**X**<sub>5</sub> is a D-or L-isomer of the amino acid serine ("S") or asparagine ("N"); or a combination thereof.

18. **(Original)** The method of claim 9, wherein the cardiac specific-synthetic expression construct comprises SeqID No: 7, SeqID No: 8, SeqID No: 9, SeqID No: 10, SeqID No: 11, SeqID No: 12, SeqID No: 13, SeqID No: 14, or SeqID No: 15.

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#### 19-28. Canceled

29. **(Original)** A method of using a cardiac specific-synthetic expression construct for expressing a gene in a cardiac cell comprising:

delivering into the cardiac cell a cardiac specific-synthetic expression construct; wherein, the cardiac-specific-synthetic expression construct comprises a cardiac-specific-synthetic-promoter (SeqID No: 5) operatively-linked to an expressible gene.

- 30. **(Original)** The method of claim 29, wherein the expressible-gene comprises a nucleic acid sequence that encodes a growth-hormone-releasing-hormone ("GHRH") or functional biological equivalent thereof.
- 31. **(Original)** The method of claim 30, wherein the encoded GHRH is a biologically active polypeptide, and the encoded functional biological equivalent of GHRH is a polypeptide that has been engineered to contain a distinct amino acid sequence while simultaneously having similar or improved biologically activity when compared to the GHRH polypeptide.
- 32. **(Original)** The method of claim 30, wherein the encoded GHRH or functional biological equivalent thereof is of formula (SEQID#6):

-X<sub>-1</sub>-X<sub>2</sub>-DAIFTNSYRKVL-X<sub>3</sub>-QLSARKLLQDI-X<sub>4</sub>-

X<sub>5</sub>-RQQGERNQEQGA-OH

wherein the formula has the following characteristics:

X<sub>1</sub> is a D-or L-isomer of the amino acid tyrosine ("Y"), or histidine ("H");

X<sub>2</sub> is a D-or L-isomer of the amino acid alanine ("A"), valine ("V"), or isoleucine ("I");

X<sub>3</sub> is a D-or L-isomer of the amino acid alanine ("A") or glycine ("G");
X<sub>4</sub> is a D-or L-isomer of the amino acid methionine ("M"), or leucine ("L");

**X**<sub>5</sub> is a D-or L-isomer of the amino acid serine ("S") or asparagine ("N"); or a combination thereof.

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- 33. **(Original)** The method of claim 29, wherein the cardiac specific-synthetic expression construct comprises SeqID No: 7, SeqID No: 8, SeqID No: 9, SeqID No: 10, SeqID No: 11, SeqID No: 12, SeqID No: 13, SeqID No: 14, or SeqID No: 15.
- 34. **(Original)** A method of using a cardiac specific-synthetic expression construct for expressing a gene in a cardiac cell comprising:

delivering into the cardiac cell a cardiac specific-synthetic expression construct; wherein, the cardiac-specific-synthetic expression construct comprises a cardiac-specific-synthetic-promoter (SeqID No: 18) operatively-linked to an expressible gene.

- 35. **(Original)** The method of claim 34, wherein the expressible-gene comprises a nucleic acid sequence that encodes a growth-hormone-releasing-hormone ("GHRH") or functional biological equivalent thereof.
- 36. **(Original)** The method of claim 35, wherein the encoded GHRH is a biologically active polypeptide, and the encoded functional biological equivalent of GHRH is a polypeptide that has been engineered to contain a distinct amino acid sequence while simultaneously having similar or improved biologically activity when compared to the GHRH polypeptide.
- 37. **(Original)** The method of claim 35, wherein the encoded GHRH or functional biological equivalent thereof is of formula (SEQID#6):

# -X<sub>-1</sub>-X<sub>2</sub>-DAIFTNSYRKVL-X<sub>3</sub>-QLSARKLLQDI-X<sub>4</sub>-

## X<sub>5</sub>-RQQGERNQEQGA-OH

wherein the formula has the following characteristics:

X<sub>1</sub> is a D-or L-isomer of the amino acid tyrosine ("Y"), or histidine ("H");

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X<sub>2</sub> is a D-or L-isomer of the amino acid alanine ("A"), valine ("V"), or isoleucine ("I");

X<sub>3</sub> is a D-or L-isomer of the amino acid alanine ("A") or glycine ("G");

X<sub>4</sub> is a D-or L-isomer of the amino acid methionine ("M"), or leucine ("L");

**X**<sub>5</sub> is a D-or L-isomer of the amino acid serine ("S") or asparagine ("N"); or a combination thereof.

- 38. **(Original)** The method of claim 34, wherein the cardiac specific-synthetic expression construct comprises SeqID No: 7, SeqID No: 8, SeqID No: 9, SeqID No: 10, SeqID No: 11, SeqID No: 12, SeqID No: 13, SeqID No: 14, or SeqID No: 15.
- 39. **(New)** A cardiac specific-synthetic promoter comprising:
- (a) a synthetic promoter element comprising c5-12 (SeqID#5), c1-26 (SeqID#16); c2-26 (SeqID#17); c2-27 (SeqID#18); c5-5 (SeqID#19); c6-5 (SeqID#20); c6-16 (SeqID#21); or c6-39 (SeqID#22); and at least one
- (b) cis-acting regulatory element comprising SRE (SeqID#1); MEF-1 (SeqID#2); MEF-2 (SeqID#3); and TEF-1 (SeqID#4).
- 40. **(New)** The cardiac specific-synthetic promoter of claim 39, wherein the synthetic promoter element comprises c5-12 (SeqID#5), and at least one cis-acting regulatory element comprising SRE (SeqID#1); MEF-1 (SeqID#2); MEF-2 (SeqID#3); and TEF-1 (SeqID#4).

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41 **(New)** The specific-synthetic promoter of claim 39, wherein the cardiac specific-synthetic expression construct comprises SeqID No: 7, SeqID No: 8, SeqID No: 9, SeqID No: 10, SeqID No: 11, SeqID No: 12, SeqID No: 13, SeqID No: 14, or SeqID No: 15.

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